Group III, claims 6-11, drawn to a method for identifying agents that increase biomarker protein level in NE-like subclone cells.

Group IV, claims 6-11, drawn to a method for identifying agents that increase biomarker mRNA level in NE-like subclone cells.

Group V, claims 6-11, drawn to a method for identifying agents that decrease biomarker protein level in NE-like subclone cells.

Group VI, claims 6-11, drawn to a method for identifying agents that decrease biomarker mRNA level in NE-like subclone cells.

Furthermore, at page 2 of the Official Action, the Examiner indicated that upon election of any of groups I-VI, Applicants are required to further elect a single species among the group of NE-1-3, NE-1-8, NE-1-9 and upon the election of any of groups III-VI, Applicants are required to further elect one of the biomarkers recited in claim 7, namely, NSE, NT, AR, PSA, EGFR, ErbB-2, ErbB-3, RPTPα, ERK1, ERK2, and MEK.

Applicants respectfully maintain that the restriction requirement set forth above is improper for failing to comply with the relevant provisions of the Manual of Patent Examination Procedures (M.P.E.P.).

Specifically, the Examiner asserts that Group I and Group II-VI are related as product and process of use and they are distinct inventions. This restriction requirement is respectfully traversed. It is clearly stated in 35 U.S.C. §121:

> If two or more **independent and distinct** inventions are claimed in one application, the Director may require the application to be restricted to one of the invention.

(*emphasis added*)

As it has been agreed by the Examiner, the subject matters claimed by Group I and Group II-VI are related. Therefore, they are **not independent inventions**. Moreover, it has been a practice within the United States Patent and Trademark Office to examine a cell line and a method of producing the same or a method of using the same in one application. For example, in U.S. Patent No. 6,410,316, an isolated retroviral vector particle producing cell and a method for producing the same are claimed; in U.S. Patent No. 6,464,973, a universal bystander cell line and a method of using the cell line for stimulating an immune response to a cancer are claimed; in U.S. Patent No. 6,316,207, a mouse cardiac muscle cell line and a method of using the cell line for screening pharmacological agents are claimed; and in U.S. Patent No. 6,284,537, an immortalized human corneal epithelial cell line and a method of using the cell line for screening a mutagenic, toxic, or beneficial agent on the metabolism of cornea cells are claimed. Therefore, it is Applicants' position that at least one if not all of the method claims should be examined simultaneously in keeping with established PTO practice as evidenced by the various patents set forth above.

The Examiner indicates that the methods of II-VI are distinct from each other because they differ at least in objectives, method steps, reagents and/or dosages, and/or schedules used, response variables and criteria for success. This restriction requirement is respectfully traversed. Again, the Examiner's attention is directed to 35 U.S.C. §121 where it is stated:

> If two or more **independent and distinct** inventions are claimed in one application, the Director may require the application to be restricted to one of the invention.

(*emphasis added*)

The subject matters claimed by Group II-VI claims relate to the process of making and process of using NE-like cells. Therefore, they are related and **not independent**. It would be improper to restrict Groups II-VI.

Moreover, MPEP §808.02 states:

> Where, however, the classification is the same and the field of search is the same and there is no clear indication of separate future classification and field of search, no reasons exist for dividing among related inventions.

Group III and V are both classified in class 435, subclass 7.1 (Official Action at page 2). There is no indication given that the field of search would be different for these inventions. If fact, one might expect the field of search to be identical, i.e., screening test compounds by observing their effects on protein levels of biomarkers. Nor is there any indication that, in the future, these two inventions would likely be searched or classified separately. Thus, there appears no basis for drawing a restriction between the inventions of Groups III and V. Likewise, the classification of Groups IV and VI are also the same, i.e., class 435, subclass 6 (Official Action at page 2). Again, the fields of search are expected to be identical, i.e., screening test compounds by observing their effects on mRNA levels of biomarkers. There is no indication that the two inventions would be searched or classified separately in the future. Therefore, there also appears no basis for requiring a restriction between Groups IV and VI.

The Examiner also states that the species cell lines, namely, NE-1-3, NE-1-8, and NE-1-9 are distinct because they have different properties. This restriction is respectfully traversed.

MPEP §806.04(f) states:

> Claims to be restricted to different species must be mutually exclusive. The general test as to when claims are restricted, respectively, to different species is the fact that one claim recites limitations which under the disclosure are found in a first species but not in a second, while a second claim recites limitations disclosed only for the second species and not the first. This is frequently expressed by saying that claims to be restricted to different species, must recite the mutually exclusive characteristics of such species.

In the instant application, the claims directed to cell lines NE-1-3, NE-1-8, and NE-1-9 do not recite exclusive characteristics. In fact, the cells lines are derived from one surviving cell after culturing androgen-responsive LNCap cells under prolonged androgen-depleting conditions. They share similar properties, i.e., similar expression patterns of NE-specific biomarkers. It is, therefore, improper to draw restriction between the subclone cell lines NE-like cells, NE-1-3, NE-1-8, and NE-1-9.

Finally, it is the Examiner's position that a restriction is required between the species biomarkers, recited in claim 7, because they are structurally distinct. Again, this restriction is respectfully traversed for the reasons set below. The species biomarkers are members of a Markush group. The Examiner is directed to MPEP §803.2 where it is stated:

> If the numbers of Markush group are sufficiently **few in number or so closely related** that a search and examination of the entire claim can be made **without serious burden**, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions.

(*emphasis added*)

In the instant case, a small number (11) of biomarkers are recited in the Markush group, namely, NSE, NT, AR, PSA, EGFR, ErbB-2, ErbB-3, RPTPα, ERK1, ERK2, and MEK. In addition, these specifies biomarkers share a common property, i.e., they are NE-specific and the expression levels are altered in NE-like cells. Furthermore, the subject matter of the claims relates to methods of assaying expression levels of NE-specific biomarkers using a novel NE-like cell line. Inasmuch as it would not pose a serious burden upon the Examiner to examine the biomarkers in one group, it is improper to require an election of a single species biomarker.

In light of the foregoing remarks, the restriction requirement of October, 1, 2002 should be withdrawn.

In order to be fully responsive to the above-mentioned requirement, Applicants hereby elect, with traverse, the subject matter of Group I for consideration in this application, which includes claims 1-4, drawn to a human prostate cancer-associated neuroendocrine (NE)-like cell line. Applicants further elect, with traverse, cell line NE-1-3 within Group I to be considered in this application. Should the Examiner agree with Applicants' request of examining at least one group of method of use claims with the subject matter of Group I, Applicants elect Groups III and V, which include claims 6-11, drawn to a method for identifying agents that modulating biomarker protein level in NE-like subclone cells. Applicants further elect, with traverse, NSE as the biomarker species within Groups III-VI to be examined in this application.

Applicants reserve the right to file one or more continuing applications, as provided in 35 U.S.C. §121, on the

subject matter of any claims finally held withdrawn from consideration in this application.

Early and favorable action on the merits of this application is respectfully solicited.

Respectfully submitted,
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